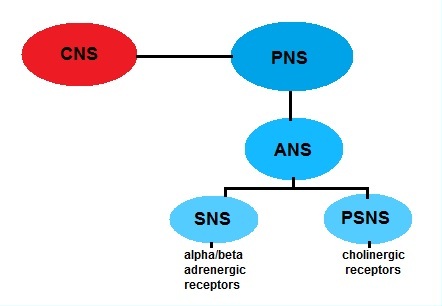
**CHAPTER 13 OUTLINE**

* Learning Objectives
  + Identify basic functions of the nervous system
  + Compare and contrast the actions of the sympathetic and parasympathetic nervous systems
  + Discuss the classification and naming of autonomic drugs based on 4 possible actions
  + For each of the drug classes, explain the mechanism of drug action and important adverse effects
  + Use the nursing process to care for patients receiving adrenergic agents, adrenergic blocking agents, cholinergic agents, and cholinergic blocking agents

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## CH. 13 – Drugs Affecting the ANS

* **The Peripheral Nervous System**(13.1)
  + Functions of the NS:
    - Recognizing internal and external stimuli
    - Processing and integrating stimuli
    - Reacting to stimuli by producing an action or response
  + Divisions of the nervous system:
    - Central NS (CNS)
      * Brain & Spinal Cord
    - Peripheral NS (PNS) (all nervous tissue outside the CNS)
      * Sensory Neurons (from sensory organs to CNS)
      * Motor Neurons (from CNS to muscles/glands)
        + Somatic NS

Voluntary control over skeletal muscle

* + - * + Autonomic NS

Involuntary control over smooth/cardiac muscle and glands

* **The Autonomic Nervous System: Sympathetic and Parasympathetic Divisions** (13.2)
  + Most organs and glands receive nerves from both divisions of the ANS
  + Divisions:
    - Sympathetic Nervous System (SNS)
      * Fight or flight
      * Activation under stressful conditions
      * Dilates pupils, inhibits salivation, accelerates heart, dilates bronchioles, inhibits digestion, stimulates release of glucose, secretes epinephrine/norepinephrine, relaxes bladder, inhibits sex organs
    - Parasympathetic Nervous System (PSNS)
      * Rest and digest
      * Activation under nonstressful conditions
      * Constricts pupils, stimulates salivation, slows heart, constricts bronchioles, stimulates digestion, stimulates gallbladder, contracts bladder, stimulates sex organs
  + ALL ANS drugs either stimulate or inhibit the ANS
    - Application: narcotics antagonize digestive function, so we already know they are either stimulating the SNS or inhibiting the PSNS….
  + These 2 divisions must be balanced to maintain homeostasis
  + They don’t always produce opposite effects – for some functions one division works entirely alone (i.e. – the SNS for vasoconstriction of arterioles and sweat glands) and for some functions both divisions work together (i.e. – male arousal and climax).
* **Structure and Function of Autonomic Synapses** (13.3)
  + Because the ANS is comprised of motor neurons, signal travels from the CNS to target muscles/glands (signal of sensory neurons would travel in the opposite direction)
  + Sequence of signal transmission:
    1. Signal travels from the cell body (ganglion) of the preganglionic nerve (which is located in the spinal cord) along its axon to the axon terminal
    2. At the axon terminal, the signal is transmitted across a synapse to the postganglionic neuron
    3. The signal travels from the ganglion of the postganglionic neuron to its axon terminal
    4. At the second axon terminal, the signal is transmitted across another synapse to the target tissue.
  + Need to review some A&P?  
    Watch this first: <http://www.youtube.com/watch?v=MUhIsrMo1K8>  
    Then this: <http://www.youtube.com/watch?feature=endscreen&NR=1&v=ZuclwAOJFh8>
  + There are 5 mechanisms by which drugs affect synaptic transmission:
    - Drugs may affect the synthesis of the neurotransmitter (NT) in the synaptic cleft
    - Drugs can prevent the storage of the NY in vesicles within the presynaptic cleft
    - Drugs can prevent the normal destruction or reuptake of the NT (indirect)
    - Drugs can bind to the receptor site on the postsynaptic target tissue (direct)
      * Therefore, they can act as agonists or antagonists to the function that would normally be performed by a NT
      * This means they stimulate or inhibit the system’s function

The classic study of drugs affecting the ANS centers around these 2 mechanisms

* + For the most part, autonomic drugs are given to correct function of target organs of the ANS, not the ANS itself
* **Norepinephrine and Acetylcholine** (13.4) ***(This section should be called NE, Epi, and Dopamine)***
  + The 2 primary NTs of the ANS are norepinephrine (NE) and acetylcholine (ACh)
  + Norepinephrine
    - Released at almost all postganglionic nerves of the SNS
    - Class of NT = catecholamines
      * Endogenous catecholamines = NE, epi, dopamine
      * Synthetic catecholamines = isoproterenol, dobutamine
    - Receptors = **adrenergic receptors**
      * **ALPHA**
        + NT = NE
        + If you stimulate an alpha-adrenergic receptor you usually get vasoconstriction and CNS stimulation
        + **alpha1**

Effects: vasoconstriction, dilation of pupils

Locations: all sympathetic organs except the heart

* + - * + **alpha2**

Effect: inhibition of release of NE

Location: presynaptic adrenergic nerve terminals

* + - * **BETA**
        + NT = Epi
        + If you stimulate a beta-adrenergic receptor you get cardiac stimulation; bronchial/GI/uterine muscle relaxation (smooth muscle); and glycogenolysis (breakdown of glycogen into glucose for fuel)
        + **beta1**

Effects: increased heart rate and force of contraction; release of renin

Locations: Heart and kidneys

(beta**1** =one heart)

* + - * + **beta2**

Effect: inhibition of smooth muscle

Location: all sympathetic organs except the heart (bronchioles, arterioles, visceral organs)

(beta**2**=two lungs)

* + - Other receptor = **DOPAMINERGIC**
      * NT = dopamine
    - Different drugs affect different combinations of these receptor types (a drug may begin to affect other receptor subtypes as the dose increases)
    - Think about the following in terms of drugs’ opportunities to affect NE:
      * Synthesis of NE requires amino acids phenylalanine and tyrosine
        + In the final step of its synthesis, dopamine is converted to NE
      * Enzymatic destruction of NE:
        + In the synaptic cleft: catecholamine-O-methyl transferase (COMT)
        + In the nerve terminal (after reuptake): monoamine oxidase (MAO)

*Ever heard of an MAO inhibitor? Now we know that its function is to prevent the destruction of NE by MAO!*

* + - * Drugs can also affect the storage, release, or reuptake of NE
  + Epinephrine
    - Adrenal medulla and SNS differentiate from the same embryonic tisse
    - Preganglionic SNS neuron terminates at the adrenal medulla and releases epinephrine into the blood
      * Epinephrine is then distributed to target organs, where it elicits fight-or-flight symptoms
      * Epinephrine’s action is terminated through metabolism by the liver
  + Dopamine
    - Has 5 receptor types (D1-D5) that have been discovered in the CNS so far
      * Important in treatment of psychosis and Parkinson’s
    - PNS dopamine receptors located in arterioles of kidneys and other organs
      * Their therapeutic importance has yet to be discovered
* **Acetylcholine and Cholinergic Transmission** (13.5)
  + Cholinergic nerves = nerves that release ACh
  + Receptors = **cholinergic receptors**
    - **Nicotinic**
      * Effects: stimulation of smooth muscle and gland secretions
      * Location: Postganglionic neurons (of both SNS and PSNS)
        + The actions of ACh in the ganglia resembles nicotine (thus the naming of nicotinic receptors)
        + These receptors are also found in skeletal muscle (the realm of the somatic NS)
    - **Muscarinic**
      * Location: Heart
        + Effect: Decreased heart rate and force of contraction
      * Location: Organs other than the heart (Parasympathetic target)
        + Effect: Stimulation of smooth muscle and gland secretions
  + Because nicotinic receptors are so widespread, drugs affecting them produce profound effects on both the autonomic and somatic divisions of the PNS.
    - Activation causes tachycardia, hypertension, and increased tone/motility in the GI tract
    - Nicotinic receptor blockers (ganglionic blockers) are currently used to relax muscles during Sx
  + Activation of cholinergic receptors affected by postganglionic nerve endings in the PSNS results in classic symptoms of PSNS stimulation:
    - Constricts pupils, stimulates salivation, slows heart, constricts bronchioles, stimulates digestion, stimulates gallbladder, contracts bladder, stimulates sex organs
    - Symptoms similar to ingestion of a poisonous mushroom called *Amanita muscaria*, thus the name “muscarinic” receptor
    - Muscarinic receptors have a number of pharmacologic applications
      * Whereas nicotinic receptors have few pharmacologic applications
  + Think about the following in terms of drugs’ opportunities to affect ACh:
    - Synthesis from amino acids choline and acetyl coenzyme A
    - Enzymatic destruction by acetylcholinesterase (AChE)
      * The resulting choline is re-used by reuptake
    - Drugs can also affect the release or receptor activation of ACh

**AUTONOMIC DRUGS**

* **Classification and Naming of Autonomic Drugs** (13.6)
  + Based on 4 possible actions:

1. Stimulation of the SNS
   * **Adrenergic agents / Sympathomimetics**
     + Produce fight-or-flight response
2. Inhibition of the SNS
   * **Adrenergic blocking agents / Adrenergic Antagonists / Sympatholytics**
     + Produce opposite effects of sympathomimetics
3. Stimulation of the PSNS
   * **Cholinergic agents / Parasympathomimetics**
     + Produce rest-and-digest response
4. Inhibition of the PSNS
   * **Cholinergic blocking agents / Anticholinergics / Parasympatholytics / Muscarinic blockers**
     + Produce opposite effects of parasympathomimetics

* What this means:
  + sympathomimetics and parasympatholytics have similar effects
  + parasympathomimetics and sympatholytics have similar effects
    - Each of these pairs typically creates effects OPPOSITE to effects of the other pair
* Tip: Memorize the function of 1 group, and extrapolate the function of the other 3 from there
* **Clinical Applications of Sympathomimetics (Adrenergic Agents)** (13.7)
  + Sympathomimetics – stimulate the SNS and produce symptoms of fight-or-flight response
  + Produce many of the same effects as anticholinergics (parasympatholytics)
    - But because the SNS has 4 subreceptor types (as opposed to only 2 for anticholinergics), the actions of many sympathomimetics are more specific and have a wider therapeutic application
  + Chemically, sympathomimetics are classified as:
    - Catecholamines
      * Same biochemical structure as NE
      * Short duration of action
      * Must be administered parenterally
    - Noncatecholamines
      * Can be taken orally
      * Have longer durations of action (because they aren’t rapidly destroyed by MAO or COMT)
  + Action of sympathomimetics:
    - Sympathomimetics act by directly activating adrenergic receptors or indirectly by increasing the release of norepinephrine from nerve terminals
      * Direct
        + Bind to and activate adrenergic receptors
        + i.e. – the endogenous catecholamines (Epi, NE, dopamine)
      * Indirect
        + Cause release of NE from its vesicles on the presynaptic neuron
        + Inhibit the reuptake/destruction of NE
        + i.e.: amphetamine, cocaine
  + Action of sympathomimetics subtypes:
    - **Alpha1**
      * Treatment of nasal congestion
      * Treatment of hypotension
      * Causes vasoconstriction, and mydriasis (dilation of pupil) during ophthalmic examinations
    - **Alpha2**
      * Treatment of hypertension (centrally acting mechanism)
        + Autonomic (peripheral) Alpha2 receptors are also located on presynaptic membranes of postganglionic neurons and serve as autoreceptors for naturally occurring NE in the SNS
        + Activation of Alpha2 receptors reduces the release of NE
    - **Beta1**
      * Treatment of cardiac arrest
      * Treatment of heart failure
      * Treatment of shock
    - **Beta2**
      * Treatment of asthma
      * Treatment of premature labor contractions
  + Examples of drugs and their receptor subtypes:
    - Epinephrine
      * Subtype – All 4 subtypes
      * Treatment – Cardiac arrest, asthma (used in anaphylaxis)
    - Pseudoepinephrine (Sudafed)
      * Subtype – Alpha1 and Beta2
      * Treatment – Nasal decongestant
    - Isoproterenol (Isuprel)
      * Subtype – Beta1 and Beta2
      * Treatment – Increases rate, force, conduction speed of the heart; sometimes used for asthma
  + Side Effects
    - Non-selective drugs generals cause more ANS side effects than selective drugs (Mostly extensions of their autonomic actions)
      * Tachycardia, hypertension, dysrhythmias
    - Large doses
      * CNS excitement, seizures
    - Also, dry mouth, nausea, vomiting.
    - Some can cause anorexia (which led to their historical use as appetite suppressants – which is considered unwise due to their CV side effects)
  + Nursing implications
    - Baseline assessment (lets you know whether a medication can be given or not… not knowing this can kill a patient)
    - Administration guidelines/routes
      * IV administration (infiltration is BAD – take care when using this route)
    - Administering 2 adrenergic agents increases cardiovascular effects – this increases the need for monitoring
    - Monitor for therapeutic and adverse effects
      * Monitor cardiac rhythm
* **Clinical Applications of Adrenergic Antagonists** (13.8)
  + Adrenergic antagonists – inhibit the SNS
  + Produce many of the same effects as cholinergic agents (parasympathomimetics)
    - COUNTERACT fight of flight mechanisms
    - Rest-and-digest symptoms
  + Wide therapeutic application in the treatment of hypertension
  + They act by directly blocking adrenergic receptors
    - Either Alpha or Beta blockers
  + **Alpha blockers**
    - AKA Ergot alkaloids
    - Relaxation of vascular smooth muscle
    - Uses:
      * Doxazosin (an Alpha1 blocker) relaxes the smooth muscle in arteries, causing vasodilation and thereby lowering blood pressure
        + Treatment of Pheochromocytoma (adrenal tumor) – this tumor increases production of epinephrine, causing hypertensive crisis, so an alpha blocker would help to reduce this
      * Also used to treat BPH (relaxation of smooth muscle in the bladder neck, prostate, and urethra)
    - Side effects:
      * Orthostatic hypotension (most common), reflex tachycardia, nasal congestion, impotence, dizziness, NVD and constipation, dry mouth
      * Effects related to increased parasympathetic activity
  + **Beta blockers**
    - All beta blockers are used for their effects on the CV system:
      * They decrease the rate and force of contraction of the heart and slow electrical conduction through the AV node.
      * They are mainly used to treat hypertension, but can also be used as a cardioprotective, and can treat migraines, angina, certain dysrhythmias, HF, MI, and glaucoma.
    - Precautions
      * Because they are used to lower blood pressure, they can lower it too much!
      * Change positions slowly, avoid caffeine, avoid alcohol and hazardous activities, report side effects, don’t stop abruptly
      * Assess history of COPD/asthma, hypotension, dysrhythmias, HF
    - Drugs that are Beta1-specific are called cardioselective because they only affect the heart (and therefore have fewer side effects), whereas drugs that affect both subtypes are called nonselective.
      * **Beta blockers atenolol, metoprolol (selective)/adverse effects:**
        + Selective = heart-specific side effect
        + Side Effects: Bradycardia, heart failure, pulmonary edema, hypotension, fatigue, dizziness, depression, lethargy, NVD (nausea/vomiting/diarrhea), impotence
      * **Beta blockers (non-selective) propranolol/adverse effects**
        + Non-selective beta blockers also affect the heart, but in addition they can cause asthma-like symptoms (due to bronchospasm)
        + Can also cause life-threatening skin side-effects (erythema multiforme, exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis)
* **Clinical Applications of Parasympathomimetics (Cholinergic Agents)** (13.9)
  + Parasympathomimetics – stimulate the PSNS and produce symptoms of rest-and-digest response
    - Increase secretions (including salivation & sweating) and peristalsis, increase urinary frequency, constrict pupils, reduce intraocular pressure
  + Acetylcholine is an NT in the SNS, PSNS, and skeletal muscle… so obviously drugs like ACh (cholinergic agents) will have widespread/varied effect**s**
  + Subclasses
    - Direct-acting agents
      * + i.e. – bethanechol (Urecholine)
      * Bind to cholinergic receptors to produce rest-and-digest response
      * They have longer-lasting effects (because they are more resistant to acetylcholinesterase (the enzyme that breaks down ACh))
      * Direct-acting agents = moderately selective = **muscarinic agonists**
    - Indirect-acting agents
      * + i.e. – neostigmine (Prostigmin)
      * They inhibit the action of acetylcholinesterase (AChE) allowing endogenous (natural) ACh to not be destroyed!
      * In other words, they help prolong the action of the body’s own ACh
      * Indirect-acting agents = nonselective = **cholinesterase inhibitors**
  + Physostigmine was first obtained from the dry, ripe seeds of *Physostigma venenosum*, a West African plant. It was originally used in tribal rituals. Then it was taken for research, and ultimately used as a template to synthesize a variety of neurotoxic substances to be used in chemical warfare. Great…
    - Today, we can find this kind of compound in organophosphate insecticides – so if we ever work in agricultural areas and encounter a patient with symptoms of acute stimulation of the PSNS, this might be the cause… Untreated, it leads to death. Antidote = atropine
  + Clinical uses:
    - Limited, due to potential for serious adverse effects
    - Ophthalmological use - Pilocarpine to treat glaucoma
    - Bethanechol used to increase bladder/GI botility (treat neurogenic bladder)
    - Used to reverse neuromuscular blocking anesthetics
    - Used to reverse anticholinergic poisoning
    - Used to treat myasthenia gravis (an AI disease which leads to destruction of nicotinic receptors in skeletal muscles)
      * Administration of cholinergic agents (pyridostigmine or neostigmine) stimulates skeletal muscle contraction, which helps reverse symptoms of severe muscle weakness
      * It can be administered before meals to help patients chew their food
    - Used to treat Alzheimer’s
      * Some drugs (donepezil and tacrine) can increase the amount of ACh binding to receptors in the CNS
    - Side Effects:
      * “SLUDGE”
      * Salivation, Lacrimation, Urinary incontinence, Diarrhea, Gastrointestinal cramps, Emesis
  + Nursing Implications:
    - Asses for GI or GU obstructions, asthma, PUD, CAD; don’t stop abruptly; spread doses evenly; overdose is life-threatening
* **Clinical Applications of Anticholinergics** (13.10) *(3 questions on anticholinergics!)*
  + Anticholinergics – inhibit PSNS impulses
  + This suppression induces a fight-or-flight response
    - Dilation of pupils, urinary retention, slowing of GI motility, increase in heart rate, drying of secretions, relaxation of bronchi
  + Historical example of an anticholinergic = belladonna “pretty woman” – women used to apply it to their faces to get rosy cheeks and dilated, doe-like eyes…
  + The most accurate term for this class is muscarinic antagonists because they are selective for ACh muscarinic receptors (and have little effect on nicotinic receptors)
  + They act directly by competing with ACh for binding muscarinic receptors
  + Therapeutic uses (try and figure out why based on known effects):
    - GI disorders, Ophthalmic procedures, Cardiac rhythm abnormalities, preanesthesia, asthma
  + Examples:
    - Atropine (prototype drug)
      * Antidote for cholinergic agent poisoning (medications/pesticides/poisonous mushrooms)
    - Deltrol
      * Helps with urinary incontinence (“Gotta-go-gotta-go” commercial)
    - Scopolamine (Hyoscine)
      * Produces sedation; prevents motion sickness
    - Benztropine (Cogentin)
      * Reduces muscular tremors/rigidity of Parkinson’s disease
    - Ipratropium (Atrovent)
      * Safer than many other anticholinergics, because it is applied as an aerosol spray (producing more local effects)
      * Used to treat COPD
  + Side Effects:
    - High incidence
    - Small doses decrease HR but larger doses INCREASE HR
    - Tachycardia, dysrhythmias, ischemia (restriction of blood supply), CNS stimulation, constipation, urinary retention in men with prostate disorders, dry mouth, dry eyes, sweating inhibition (heat stroke!), photophobia (due to pupil dilation), decreased bronchial secretions
    - Overdose (anticholinergic crisis) symptoms:
      * Fever, visual changes, difficulty swallowing, psychomotor agitation, hallucinations
      * “Hot as hades, blind as a bat, dry as a bone, mad as a hatter.”
  + Nursing Implications:
    - Assess for allergies, BPH, glaucoma, tachycardia, MI, CHF, hiatal hermia, GI or GU obstruction
    - Take baseline VS
    - Overdose can be life-threatening
    - Blurred vision side effect can be dangerous if driving/operating machinery
    - Apply sunglasses/sunscreen for photosensitivity
    - Apply pressure to inner canthus (the medial corner of the eye over the nasolacrimal duct) to prevent systemic absorption
    - Monitor side-effects
  + Contraindications:
    - Glaucoma, acute hemorrhage, tachycardia, GI obstruction